REMARKS

Claims 11 and 28-30 are pending, and all the pending claims are rejected. The Examiner's positive views regarding patentability under 35 U.S.C. § 102 and 103 are acknowledged and appreciated.

Regarding the Information Disclosure Statement

Applicant submits herewith a hard paper copy of the voluminous WO 01/22920A2 since a CD copy is not acceptable.

Rejection under 35 U.S.C. § 112, first paragraph

Claims 11 and 28-30 are rejected as not properly enabled. The Examiner says that neither the specification nor the literature provides any evidence that an antibody to NKCC1/SEQ ID NO:1 would treat breast, lung or pancreatic cancer. The Examiner cites recent U.S. case law for the proposition that while it might not require a lot of experimentation but only routine screening to make and isolate antibodies to NKCC1, it would require undue experimentation to find an antibody to NKCC1 that would be effective to treat breast, lung or pancreatic cancer.

1. <u>All the steps required to practice the claimed invention short of actual therapy are clearly and unquestionably enabled.</u>

The Examiner acknowledges that the specification teaches techniques for:

- the production of antibodies that bind to an antigen immunospecifically,
- methods of selecting antibodies for therapeutic use, and
- antibody-drug conjugation techniques

but then continues that the specification must contain the manner for making and using the invention. In particular, according to the Examiner, screening assays do not enable the claimed invention (*citing, University of Rochester v. G.D. Searle* 358 F.3d. 916, Fed. Cir., 2004) because they are merely a wish for a **chemical** invention [emphasis added]. Current claim 11 is directed to a method of treating beast, lung and/or pancreatic cancer employing a monoclonal, chimeric, humanized or completely human antibody that specifically binds to the protein NKCC1. Claim 28 depends on claim11 and is limited to where the antibody is a conjugate with certain chemical

entities.

Applicant respectfully directs the Examiner's attention to Example 3 in the specification as filed. Example 3 provides details of immunohistochemistry performed on breast cancer, pancreatic cancer and lung cancer tissue. The Examiner is respectfully reminded that immunohistochemistry staining employs an antibody conjugated to a chemical stain. When the antibody binds to a protein to which it is specific (in the instant invention, NKCC1), the relevant tissue is stained. Example 3 indicates that NKCC1 immunostaining was seen in breast cancer tissue and it was clearly apparent that NKCC1 is specifically and highly expressed in ductal carcinoma cells of the breast cancer tissue (compared with adjacent breast tissue). Of course all breast cancers are not of the same source or type, and out of 55 samples, 5 samples did not show staining. However, this is to be expected in the field. For example, in known breast cancer adjuvant therapies such as tamoxifen, certain patients are more suitable for treatment with the product than others. The most suitable cancers for treament are those with estrogen receptors on the surface of their cells, termed 'estrogen-receptor-positive' (ER-positive). This does not reflect negatively upon the value of the therapy. In a separate example Her-2/neu expressing breast cancer is suitable for treatment with the pharmaceutical product Herceptin.

Example 3 further teaches that increased staining of sections for NKCC1 was seen in both lung and pancreatic tissue sections in comparison to adjacent control sections. Thus, Example 3 provides evidence of the increased expression of the protein in the cancerous tissue and the ability of antibodies specific to NKCC1 to bind to the protein in tissue.

Methods for making, screening and administering antibodies were routine in the art at the time the instant application was filed, and the association between the specific diseases is taught in the instant specification as filed. Yet, the Examiner maintains the rejection that the present specification does not teach how to make and use the invention as claimed, relying upon the decision of the Federal Circuit in *University of Rochester v. G.D. Searle, supra.*

2. The facts of the controlling case law cited are clearly distinguishable.

Applicant respectfully submits that the facts of *University of Rochester v. G.D. Searle* are distinguishable in many ways. The *University of Rochester v. G.D. Searle* related to **reach through** claims, i.e. claims to **chemical** compounds identified in a screening method. The court concluded that, as a matter of law, the patent at issue was invalid because a required compound

was not disclosed and there was no pre-existing awareness in the art of such a compound exhibiting the claimed activity. Applicant submits that an important factor in the case is that it was not known how to make a selective COX-2 inhibitor when the application was filed. That is, in the *University of Rochester v. G.D. Searle* situation, knowing what the target receptor was provided little assistance to a skilled person to design a new chemical entity that that modulated the activity of the receptor.

The facts of the present invention are distinguishable in several respects:

1. The pending claims are not reach through claims but rather claims relating to a method of treatment;
2. Antibodies to the target protein were known before the instant application was filed and are exemplified in the application as filed;
3. One of ordinary skill in the art is able to prepare and screen other antibodies by well known techniques;
4. Once one of ordinary skill in the art has the antigen, antibodies to the antibody can be prepared without undue experimentation because there is a functional relationship between the two;
5. In the instant application as filed, binding in certain cancerous tissue and lower levels of expression of the relevant protein in healthy tissue is shown; and
6. One of ordinary skill in the art could administer the antibodies in a method of treatment in light of the teachings of the instant specification without undue experimentation, for example by infusion or vaccination.

3. Antibody technology is relatively predictable.

Applicant submits that the Examiner's comment that screening assays do not enable the claimed invention (*citing, Rochester v Seale* 358 F.3d. 916, FED Cir., 2204) because they are merely a wish for a **chemical** invention, are merely reflective of novel chemical entities. The Examiner's reasoning is not applicable to antibodies, which are a specific class of biological molecules.

Applicant submits that the teachings of the present specification meet the requirement of 35 U.S.C. § 112 as regards method of treatment claims. In particular, it has never been the law

that clinical data must be available to meet the enablement requirement of 35 U.S.C. § 112. Applicant respectfully reminds the Examiner that in *Glaxo v. Teva* (2004 WL 1875017 D. Del 2004), the court concluded that there is no requirement in the law for working examples. Thus the fact that there is no clinical data in the specification does not render a rejection under 35 U.S.C. §112 proper.

The Examiner asserts that the development of novel cancer therapeutics is unpredictable and thus this results in a failure to meet the criteria set of 35 U.S.C. § 112. Applicant agrees that in some instances the development of novel cancer therapeutics is unpredicatable. However, Applicant submits that antibodies are distinguishable from simple new chemical entities (i.e. compounds which are simply inhibitors). Much of the case law relates to such new chemical entities. This distinction can be drawn in part due to the high specificity of antibodies to the target protein and the functional interrelation of an antibody and a target protein. In support of this fact, Applicant submits two articles herewith, discussing the success rate of antibody pharmaceutical products, Ziegelbauer *et al., Journal of Commercial Biotechnology* 14(1):65-72 (2008) and Reichert *et al., Drug Discovery* 3:383 (2004). In particular Zeigelbauer *et al.* teach as follows:

> "Therapeutic antibodies have a high drug approval success rate once they reach clinical testing (29 percent for chimeric antibodies, 25 per cent for humanized antibodies compared to a success rate of approximately 11 per cent for small molecules).[7] In addition, much of the development and clinical experience that is gained from the generation and optimization of one antibody product can be readily applied to subsequent therapeutic antibodies, diminishing some of the development, manufacturing, and clinical risks that are intrinsic to drug development.
>
> Owing to their exquisite specificity and ability to affect unique biological functions, monoclonal antibodies have the potential to provide a continued source of effective, safe, and reliable therapies. The introduction of such new therapies will benefit patients having a variety of debilitating diseases that otherwise respond poorly to alternate approaches. Based on the impact of the successful discovery of novel antibody functions on the current portfolio of antibody drugs, it is likely that the ability to continue to engineer novel functionalities by using new antibody formats will drive the expansion of the antibody drug market in the future."

Applicant submits that biological type products are much more likely (perhaps 4 or 5 times more likely) to be commercialized than a new chemical entity. Applicant submits that this in part is due to the specificity of antibodies in a biological context. Thus, relatively speaking,

Applicant submits that the unpredictability in the field under consideration is lower (perhaps significantly lower) than in other therapeutic fields.

4. The USPTO guidelines for determining whether a specification is enabling for the claimed invention recognize that the specific facts and the state of the art must be considered in each instance such that no absolute rule exists.

Applicant respectfully directs the Examiner to USPTO educational materials provided in a presentation by Jean Witz http://www.cabic.com/bcp/031208/JWitz_ECTT.ppt, a copy of which is enclosed. The USPTO educational materials indicate that:

- That the amount of guidance or direction required to enable an invention is inversely proportional to the amount of knowledge in the art (and we know the skilled person in the biotech field is highly skilled);
- All the evidence must be weighed up by the Examiner;
- There are no rules *per se* (i.e., that apply unilaterally across the board); and
- The analysis should be performed on a case-by-case basis.

Applicant further reminds the Examiner that the Examiner has the initial burden to establish a reasonable basis to question the enablement provided, that there must be a reason to doubt the objective truth of the statements contained in the specification, that references should be supplied if possible to support a *prima facie* case of lack of enablement, and that specific technical reasons (to support a *prima facie* case of lack of enablement) are always required. Applicant respectfully submits that the Examiner has failed to establish such a reasonable basis to question the enablement provided. Further, the Examiner has not established specific technical reasons to support the allegation that the specification does not enable the methods of treatment claimed. Still further, the Examiner has provided no references supporting such an allegation.

Applicant further submits the following points:

- The present claims are not directed to a **cure** for the particular cancers but are claiming a method of treating certain cancers. Even established treatments including chemotherapy and radiotherapy are not successful in one hundred percent of cases but are still valid methods of treatment.

- The claimed treatment may ultimately need to be used in combination with other treatments in a cocktail (this does not undermine the value of the present treatment as a component of same).
- Given antibodies have been shown to bind to the cancerous tissue expressing the relevant protein, the known antibodies could be used to at least some extent.
- Whether certain products make it to the market is sometimes a commercial decision based on a number of factors including the timing to the market and resources to support projects and therefore products that make it to market is not a good indication of unpredictability in the art.

Respectfully, Applicant submits that one of ordinary skill in the art could make and use a "method of treatment..." according to the present claims without undue experimentation. Hence, a rejection under 35 U.S.C. §112, first paragraph as regards enablement is improper.

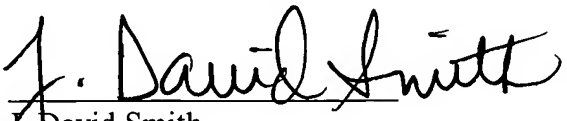
Fees

No additional fees are believed to be necessitated by the present Response. However, should any fees be due, authorization is hereby given to charge Deposit Account No. 11-1153 for any underpayment, or credit any overages.

Conclusion

It is believed that the claims are in condition for allowance. In the event that there are any issues that may be resolved by telephone, the Examiner is respectfully urged to call the undersigned at the telephone number indicated below.

Respectfully submitted,



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